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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/216,506	03/22/94	SCHLEGEL	C 010091001

EXAMINER
CAPUTA, A

18N1/0408

ROBIN L. TESKIN
BURNS, DOANE, SWECKER & MATHIS
P.O. BOX 1404
ALEXANDRIA, VA 22313-1404

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/216,506	Applicant(s) Schlegel et al.
	Examiner Anthony C. Caputa	Group Art Unit 1806

☒ Responsive to communication(s) filed on *10/13/95; 11/6/95; 1/19/95*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-3, 10-19, 21-26, 46, 47, and 50-63* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-3, 10-19, 21-26, 46, 47, and 50-63* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Part III DETAILED ACTION

1. Applicants' amendments and declaration were received and been have entered. Claims 4-9, 20, 27-45, 48, and 49 have been canceled. Claims 1-3, 10-19, 21-26, 46, 47, 50-63 and are pending.

2. The text of those sections of Title 35 U.S.C. not included in this action can be found in a prior Office Action.

3. The prior rejection of claim 20-26 under 35 U.S.C. § 112, second paragraph, for lack of antecedent basis for the term "animal" is withdrawn in view of applicants' amendment.

4. The prior rejection of claims 1-3, 10-12, and 15 under 35 U.S.C. § 102(b) as being anticipated by, or, in the alternative, under 35 U.S.C. § 103 as obvious over Browne et al. (Journal of General Virology 69(6): 1263-1273) or Minson et al. is withdrawn.

The declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 is sufficient to overcome the rejection of claims 1-3, 10-12, and 15 based upon the disclosure of Browne et al. (Journal of General Virology 69(6): 1263-1273) or Minson et al.

5. The prior rejection of claims 13, 14, 16-26, 46, 47, and 50-58 under 35 U.S.C. § 103 as being unpatentable over Browne et al. as applied to claims 1-3, 10-12, and 15 above, and further in view of Danos et al. (US Patent No. 4,551,270) is withdrawn.

The declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 is sufficient to overcome the rejection of claims 13, 14, 16-26, 46, 47, and 50-58 based upon the teachings of Browne et al. (Journal of General Virology 69(6): 1263-1273) and further in view of Danos et al. (US Patent No. 4,551,270).

6. Claims 1-3, 10, 12, 15, and 59-62 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Carter et al. as set forth in the last Office Action.

As set forth previously,

Carter et al. disclose the L1 open reading frame of human papillomavirus types 1 and 16 has been expressed in yeast (see abstract and page 515). Carter et al. does not characterize the recombinantly L1 protein as having the same properties as the claimed L1 protein (i.e. reproducing the antigenicity and conformation of the L1 on the native virus). Nevertheless, it is reasonable to conclude the protein as set forth by Carter et al. inherently has the same properties as the claimed protein since both the claimed protein and protein set forth by Carter et al. are a human papillomavirus L1 protein produced recombinantly. Furthermore, it is reasonable to conclude the protein as set forth by Carter et al. inherently, or in the alternative has the same properties as the claimed protein (i.e. reproducing the antigenicity and conformation of the L1 on the native virus) since the L1 of HPV when expressed in yeast was identical in size the purified proteins in size and were recognized by monoclonal antibodies generated against the HPV virion (See page 520).

Carter et al. does not teach of the recombinant L1 produced by the same expression system (i.e. baculovirus) as claimed. However, while the proteins of the reference was not obtained from the same expression system, they nevertheless appear to be the same or an obvious or analogous variant of the proteins broadly and non-specifically claimed by applicants because they appear to possess the same or similar functional characteristics, i.e. a human papillomavirus L1 protein produced recombinantly. The source of a particular protein does not impart novelty or unobviousness to a particular protein when said protein is taught by the prior art. Since the Patent Office does not have the facilities for examining and comparing applicants' proteins with the proteins of the prior art reference, the burden is upon applicants to show an unobvious distinction between the material structural and functional characteristics of the claimed proteins and the proteins of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Although the reference appears to disclose the same protein claimed by applicants, the reference does not disclose the proteins **produced** by the claimed process. However, the production of a protein by a particular process does not impart

novelty or unobviousness to a protein when the same protein is taught by the prior art. This is particularly true when the properties of the protein are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular **process** used to prepare a protein is novel and unobvious over the prior art, the protein per se, even when limited to the particular process, is unpatentable over the same protein taught by the prior art. See In re King, 107 F.2d 618, 620, 43 U.S.P.Q. 400, 402 (C.C.P.A. 1939); In re Merz, 97 F.2d 599, 601, 38 U.S.P.Q. 143, 144-45 (C.C.P.A. 1938); In re Bergy, 563 F.2d 1031, 1035, 195 U.S.P.Q. 344, 348 (C.C.P.A. 1977) vacated 438 U.S. 902 (1978); and United States v. Ciba-Geigy Corp., 508 F. Supp. 1157, 1171, 211 U.S.P.Q. 529, 543 (D.N.J. 1979).

Carter et al. does not characterize the L1 as being useful as a vaccine. However, it is the Examiner position the claim directed to a vaccine comprising the L1 is anticipated, or rendered obvious over the L1 as set forth by Carter et al. since the intended use of the claimed composition does not carry any patentable weight.

The declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 is sufficient to overcome the rejection drawn to the L1 species of HPV-16 encompassed in claims 1-3, 10-12, and 15 based upon the disclosure of Carter et al.

However, the declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 and applicants arguments are **not** sufficient to overcome the rejection drawn to the L1 species of HPV-1 encompassed in claims 1-3, 10, 12, and 59-62 based upon the disclosure of Carter et al.

Applicants set forth in the declaration and arguments that the L1 of HPV-1 would not have the proper confirmation since PCR would have likely resulted in mutations. Applicants arguments are not persuasive since while it may be true that a DNA of 1500 nucleotides on average would have 3 to 5 mutations there is no evidence the DNA as set forth by Carter has any mutations. Beyond this assuming there is a mutation(s) as argued by applicants since mutations are known to be silent, result in a

conservative substitution, or result in in an amino acid change which does not result in a conformation change it is not expected that a mutation results in a conformation change as argued by applicants. Accordingly, for the reasons set forth above and in the last Office Action said rejection is maintained.

Applicants' arguments and declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 with respect to the truncated L1 of HPV-6b has been considered but is deemed to be moot in view the rejection of claimed invention over the disclosure of Carter et al. as set forth in the previous Office Action was directed to the L1 of HPV-1 and 16 and not the truncated L1 of HPV-6b.

7. Claims 13, 14, 18, 19, 21, 25, 46, 47, 50, 51, 53, 54, and 59-62 are rejected under 35 U.S.C. § 103 as being unpatentable over Carter et al. as applied to claims 1-3, 10, 12, 15, and 59-62 above, and further in view of Danos et al. (US Patent No. 4,551,270) as set forth in the last Office Action.

Carter et al. teachings are set forth above. Carter et al. does not teach of a method of protecting a human against a papillomavirus infection using the L1.

Danos et al. (US Patent No. 4,551,270) teach sequences containing the L1 region are capable of producing antibodies which are able to neutralize HPV (see Columns 3 and 7). Danos et al. teach the vaccine can be administered orally or parenterally.

It would have been obvious to one of ordinary skill in the art to use the L1 as set forth by Carter et al. as a method of protecting a human against a papillomavirus infection since Danos et al. teach sequences containing the L1 region are useful as a vaccine (see Columns 3 and 7). It would have been obvious to one of ordinary skill in the art to optimize the dosage to provide the greatest protection against infection. It would have been obvious for one of ordinary skill in the art at the time of the invention to use the HPV types (i.e. HPV 18) known in the art to protect against infection by the respective HPV since Browne et al. teaches different HPV types are associated with different clinical signs (i.e. HPV 16 and 18 are associated with cancerous and precancerous lesions and HPV 6 and 11 are associated with benign condylomas). It would have been further obvious to one of

ordinary skill in the art to include a vaccine composition which contain the L1 of several types of PV since one would have been motivated to provide protection against several types of PV described in the art.

Danos et al. (US Patent No. 4,551,270) teach (see Column 6) L1 peptides coupled to a carrier such as serum albumins preferably animal for use as a vaccine. It would have been obvious to couple L1 with serum albumins as described by Danos et al. (US Patent No. 4,551,270) such as bovine serum albumin, a serum albumin well known in the art to enhance immunogenicity of the L1.

The declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 is sufficient to overcome the rejection of drawn to the L1 species of HPV-16 encompassed in claims 13, 14, 17-19, 21, 22, 26, 47, 50, 51, 53, and 54 under 35 U.S.C. § 103 as being unpatentable over Carter et al., and further in view of Danos et al. (US Patent No. 4,551,270).

However, the declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 nor applicants arguments are not sufficient to overcome the rejection drawn to the L1 species of HPV-1 encompassed in claims 13, 14, 18, 19, 21, 25, 46, 47, 50, 51, 53, 54, 59-62 under 35 U.S.C. § 103 as being unpatentable over Carter et al., and further in view of Danos et al. (US Patent No. 4,551,270).

The rejection of claims 16, 23, 24, 52, 55, and 56-58 over the teachings of Carter and further in view of Danos et al. is withdrawn upon further consideration by the Examiner since the L1 claimed is of a HPV not taught by Carter (i.e. HPV-18).

Applicants appear to argue that Danos et al. teachings are not sufficient to make obviousness type rejection since Danos et al. "prophetically describes that these peptides may potentially be useful for protecting hosts against papillomavirus infection" (see page 11 of Paper No. 26). Applicants statements are not persuasive to overcome the rejection since a U.S. Patent has a

presumption of validity under 35 USC 282. Applicant state "As previously established linear HPV 1 proteins nor peptides are useful for use as HPV vaccines" (see page 19 of Paper No. 26). Applicants arguments are noted. However, since applicants have failed to indicate were in the record or in the art it has been previously established that linear HPV 1 proteins and peptides are not useful as a vaccine applicants statement is not sufficient to overcome the rejection.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 112/1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach one of ordinary skill in the art how to make and/or use the claimed invention, i.e. failing to provide an enabling disclosure.

The specification is not enabled to make a L1 protein from HPV-16 which has the features as claimed.

From applicants arguments and declaration by Drs. Schelegel and Jensen under 37 C.F.R. § 1.132 filed 10-30-95 it would appear that the L1 from the prototype of HPV-16 used in the art at the time of the invention (i.e. Minson et al., Browne et al., Zhou et al., etc.) does not have the properties as the L1 as claimed. Since the specification provide no direction of what HPV-16 is to

be used to make the L1 as claimed, and the HPV-16 available at the time of the invention does not produce the L1 with the properties as claimed it would be an undue burden for a skilled artisan to make and use the L1 of HPV-16 encompassed in the claimed invention.

10. Claims 10, 11, 15, 17, 18, 21, 22, 26, 51, 54, and 63 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

11. The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification as originally filed does not provide support for the invention as now claimed.

The specification as originally filed does not provide support for a L1 that reproduces the antigenicity of ....intact, native (or mature) human papillomavirus. At best the original claims provides support for a L1 which mimics the conformation of an intact virus particle (see page 9, last paragraph, and claim 12) and not intact native (or mature) human papillomavirus. Since there are no blazemarks for the terms "native" or "mature" in the specificiation nor how said terms define the metes and bounds of the claimed subject matter it is the Examiner's position the specification as originally filed does not provide support for the invention as now claimed.

12. Claims 1-3, 10-19, 21-26, 46, 47, 50-63 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

13. Claims 1-3, 10-19, 21-26, 46, 47, 50-63 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for

failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 10-19, 21-26, 46, 47, 50-63 are rejected for using the term "native" and "mature" since it is not clear how said terms further define the metes and bounds of the claimed subject matter.

14. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ghim et al. (Virology 190: 548-552 September 1992) teach (see abstract) of polyclonal and monoclonal antibodies which react specifically with conformational epitopes of the HPV-1 L1 protein. Ghim et al. teach the screening of capsid protein of PV for reactivity with conformation dependent antibodies represents a method to ensure that such proteins will be suitable for vaccine development or detection of human PV infections.

Danos et al. teach the DNA sequence encoding the L1 of HPV1a.

Schwarz et al. teach the DNA sequence encoding the L1 of HPV6b. Cole et al. (1986) teach the DNA sequence encoding the L1 of HPV33. Cole et al. (1986), Schwarz et al. further teach the strong identity (i.e. homology) of the DNA encoding the L1 of the various PV's.

Seedorf et al. teach the DNA sequence encoding the L1 of HPV16.

Baker et al. teach of the DNA sequences of the L1 of various papillomaviruses and the that DNA sequences of various papillomaviruses are available (see whole document especially page 321, Figure 17. Baker et al. teaches of using methods known in the art to determine the ORF's of particular protein including L1. Baker et al. teaches the L1 are the most highly conserved of the papillomavirus proteins (see page 379, first paragraph).

Cole et al. (1987) teaches of the DNA sequence of the L1 of HPV 18 and homology of the L1 of the various PV's.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Anthony C. Caputa, whose telephone number is (703)-308-3995. The examiner can be reached on Monday-Thursday from 8:30 AM-6:00 PM. The examiner can be reached on alternate Fridays. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist,whose telephone number is (703)-308-0196.

Papers related to this application may be submitted to Group 1806 by facsimile transmission. Papers should be faxed to Group 1806 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the official Gazette 1096 OG 30 (November 15, 1989). The CMI Fax Center number is (703)-305-7939.

Anthony C. Caputa, Ph.D.
April 1, 1996

ANTHONY C. CAPUTA
PATENT EXAMINER
GROUP 1800